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ETIOLOGY OF APPENDICITIS

WHY IS IT MORE COMMON IN THE ANGLO-SAXON RACE?

BY

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WHY IS IT MORE COMMON IN THE ANGLO-SAXON RACE?

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I dislike to preface a paper with an apology, but I feel that I am taking an undue advantage of my guests in inflicting upon them a paper of this length with its somewhat tedious recital of details, with which many of you are doubtless familiar, without a word in extenuation.

When I entered the ranks of the profession, seven years ago, the importance of the appendix as a factor in the production of inflammatory affections of the peritoneum was just beginning to be generally recognized.

We need not go back to even so recent a period to recall earnest discussions over the very existence of the appendix as an intraperitoneal structure, or the more heated arguments as to the necessity, or not, of surgical interference in any case of appendicitis.

The whole subject of appendicitis has been so earnestly and thoroughly worked over in this society since that time, and our ideas have undergone such a rapid and continuous process of evolution that we have been all but ready to declare the argument closed. However, at least so far as the etiology is concerned, I am becoming more and more convinced that this evolutionary process has been too rapid to thoroughly eliminate the "unfit," and I present this paper for the purpose, first, of reviewing the evidence upon which our present opinions are based; second, of introducing new evidence, direct and circumstantial; third, of obtaining a candid criticism of this evidence, the deductions that I have drawn from it, and of theories which seem to me plausible.

It is not without some diffidence and hesitation that I present this paper to the Louisville Surgical Society, realizing only too well its imperfections.

The explanations that I have suggested of some of the more important phenomena noted in connection with this subject are

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in my opinion justified by the data at our command, but these data are insufficient to justify any sweeping generalizations. I have purposely avoided any detailed report of personal cases, which from the very nature of things can only in exceptional instances be more than corroborative, and whether future observations confirm the opinions expressed herein or not, I am satisfied that a more extended investigation of the etiology of appendicitis along the lines suggested will amply repay us.

That we may fully appreciate all the factors concerned in this complex disease process which we term appendicitis, let me briefly recall to your mind the more salient features in the anatomical relations of this organ as well as its histological structure. The appendix vermiformis, the atrophied remnant of the true cecum, is found attached to what was originally the apex of the cecum, usually on the inner and posterior aspect of the bowel, close to the ileo-cecal valve. The relative position of the appendix is subject to many variations, which have not, however, been shown to bear any constant relation to disease of this structure. The appendix varies, likewise, in length and caliber in individuals, in the male and female, and at different periods of life. Its length will average at its greatest development from three to four inches, being four-fifths inch longer in male than the female. It is usually entirely invested by peritoneal folds derived from the inferior layer of the mesentery of the ileum; these folds forming as a rule a triangular mesentery for the appendix, the base of the triangle being formed by the free edge of the folds. The attachment of this meso-appendix may extend along the entire length of the appendix, more often only to the proximal two thirds; more rarely the meso-appendix is absent and the appendix floats freely in the abdominal cavity.

The appendix is commonly found curved upon itself, owing to the shortening of its mesentery. Along the free edge of this meso-appendix runs the appendicular artery, the essential nutrient artery of the appendix. It is a terminal branch given off from an anastomotic loop, formed by the superior mesenteric and the ileo-colic; and where the mesentery is absent it runs beneath the peritoneal coat of the appendix.

The lymphatics of the appendix pass into the appendicular lymphatic ganglion, which lies in the angle formed by the ap-

pendix and the cecum. In the female lymphatic channels pass along the appendiculo-ovarian ligament between the folds of the peritoneum, forming this structure and establishing communication between the appendix and ovary. (Clado.)

The nerve supply of the appendix is derived from the superior mesenteric plexus of the sympathetic through filaments given off by the branch accompanying the ileo-colic artery.

The appendix is made up of four layers: (1) A more or less complete covering of peritoneum which we have noted. (2) A muscular coat made up of two layers, an outer portion consisting of a few long non-striated muscular fibers mingled with a varying amount of fibrous tissue and an inner portion of circular fibers, thicker and more regularly distributed than the outer. (3) The submucosa, a thick layer formed of areolar tissue, containing numerous lymphoid glands, and through which ramify numerous small arteries and veins supplying the mucous membrane; between this layer and mucous membrane a thin layer of circular muscular fibers may be distinguished, the muscularis mucosæ. (4) The mucous coat is composed of a delicate rectiform tissue, with a basement membrane, lined with columnar epithelial cells. It contains in its meshes numerous lymphoid cells and has dipping into it a number of mucous glands. About the orifice of the appendix the lymphoid tissue is oftentimes deposited in increased amount and may partially obstruct the opening. I have not attempted, in thus running over the anatomy of the organs, to more than refresh your memories on the more salient points.

The earlier observers looked upon foreign bodies as the chief factors in the production of appendicular disease, but this idea has not been borne out by more extended experience, as they have been found in only about four per cent. of operative cases. They may act, however, by producing abrasions of the mucous membrane and opening an avenue of infection by mechanically interfering with the exit of the mucous secretion from the appendix, or by direct pressure effects interfere with the nutrition of the organ and bring about necrosis.

Fitz, in his paper, laid special stress on the influence of fecal concretions as most frequently causing disease of the appendix, and this view has been very generally accepted. On close

investigation this seems to be a very questionable matter. [1]Klebs, in an examination of four hundred specimens, concludes that the vermiform appendix has usually very little contents, which he attributes to the fact that the normal musculature regularly voids its contents. He found fecal stones in thirty-eight of the four hundred specimens, and equally in both sexes; this tallies with the reports of other observers. These stones have been found repeatedly in appendices in which their presence had given rise to no imflammatory action, and moreover have only been found in about fifteen or twenty per cent. of operative cases of appendicitis. The evidence tends to show that these fecal stones form in the appendix from the absorption of the liquid portion of the fecal mass, and as the result of the inability of the appendix to normally void its contents; and while it is not questioned that by these pressure effects necrosis and infection may be brought about, their very presence in the appendix presupposes an inability of the appendix to empty itself. If this were due to lack of development of its muscular coat, it should be manifested in very early life, otherwise the natural presumption would be that some alteration in the structure of the appendix must take place, interfering with the evacuation of its contents, and clinical experience has shown stricture of the appendix to be a frequent source of trouble. Another possible element in the production of appendicitis, to which I have called attention several times, is the overdistension of the appendix by gas or fecal matter during violent muscular efforts; given a colon distended with gas and fecal matter, it is not difficult to understand how the increased pressure brought about by lifting or straining at stool, coughing, vomiting, etc., might forcibly distend the appendix and produce sufficient trauma to start an inflammatory process.

Another source of appendiceal trouble, although doubtless not a frequent one, lies in the extension of an inflammatory process to the appendix from other organs by continuity or contiguity of tissue. That a catarrhal or ulcerative process beginning in the cecum may extend thence to the appendix, or that an appendix becoming adherent to diseased pelvic organs may become thus secondarily infected, is unquestionable.

[1]Annual of the Universal Medical Sciences, 1894.

From a *practical* standpoint the *most important* factors in the *development* of appendicitis are the *pathogenic bacteria*, and of these the colon bacillus seems to be most in evidence. It is almost invariably found in the intestinal tract, and in the presence of sound mucous membrane seems to be without power for evil. However, when the mucous membrane has been destroyed, or the intestinal canal has been subjected to constriction and its circulation interfered with, the colon bacillus may penetrate the intestinal wall and show both pathological and pyogenic properties. It has been found in almost all cases of perforative appendicitis, frequently alone, sometimes associated with other pus-forming organisms. Typhoidal and tubercular ulceration have also been observed in the appendix in a not inconsiderable number of instances.

A most fertile source of appendix trouble is believed by most authorities on this subject to exist in a special liability of the appendix to nutritive disturbances, from *interference* with its *blood supply*, by an *insufficient mesentery* or by *torsion*. This point is especially dwelt upon by Fowler in an exhaustive report of his [2] "Observations Upon Appendicitis." In answer to the question, Why, if the same pathological laws govern the tissues of the appendix that govern the other tissues of the body, do they assert themselves so much more frequently here than elsewhere? he says there is one prime factor which more than any other is responsible for this fact, to wit, that here, as nowhere else certainly in the abdominal cavity, the parts are peculiarly exposed to circulatory and hence to nutritive disturbances. Prof. Van Cott's careful examination of many specimens furnishes convincing proof that vascular and nervous lesions are important factors to ultimate disease of the appendix. In addition to this, proof is furnished by the interesting fact that females are less frequently stricken with the disease than males; and that, as already stated, in the female sex an extra supply of blood is furnished to the appendix through the medium of the appendiculo-ovarian ligament, a fact bearing notably on the question of nutrition. In all of the specimens examined, thirteen in number, there was revealed the presence in the mesenteric vessels of some form or other of obstruction to the

[2] Annals of Surgery, 1894.

blood current, either endo-vasculitis or organized thrombus, conditions which must in the nature of the case have long preceded the intense, small round-cell infiltration, coagulation necrosis and purulent foci present in the walls of the appendices themselves. In several cases, in addition, a distinct neuritis interstitialis chronica supervened; in one, the hyperplastic endo- and perineurium being so abundant as to have caused extensive atrophy of the nerve fibers. It is indisputable that such lesions of vessels and nerves can only result ultimately in a most profound disturbance of the appendical tissues, with lessened resistance and localized necrosis. Why the appendix, for example, should be free from the consequences of anemic infarct so certain in the renal and other tissues endowed with a terminal circulation, is difficult to comprehend. On the other hand, if the trophic fibers which must exist in the nerves of the meso-appendix be subjected to pressure through hyperplasia of their connective tissue sheath to the extent of causing atrophy, trophic changes must necessarily occur in the appendix itself, and will be co-extensive with the nerve lesion.

Assuming the correctness of these conclusions, it is evident that two things are possible: (1) That the real cause of the locus minoris resistentiæ, which admits of bacterial infection of the appendix, must be sought, not in trauma of the mucosa but rather in trophic disturbances of the appendix, resulting from (*a*) chronic vascular lesion, (*b*) chronic nervous lesion, or (*c*) both of these combined; and (2) that this trophic disturbance will be intense or moderate, depending upon the nature of these lesions Hence it must follow that ulcerative processes in the appendix, while they may be increased by bacterial invasions, may, nevertheless, owe their origin to the trophic conditions. Therefore it must always be difficult to prove that a given ulcerating process or pus-focus in the appendix is due to bacterial invasion primarily, and the more especially is this true when lesions of the vessels and nerves of the mesentery obtain. It would seem much more cogent reasoning to assume that bacterial invasions were made possible by the lessened resistance of the part through defective nutrition than that primary necrosis is the result of direct invasions of germ through a normal mucosa.

The American Text-Book of Surgery, after noting the rela-

tions of the peritoneum to the appendix, says: "We have here the factors which enter into the production of a large number of cases of appendicitis; distension of the caput-coli with gas or fecal matter will cause dragging on one or the other of the folds already too scanty, increase the torsion of the appendix, interfere with its blood supply through its single vessel, and according to the degree of torsion produce congestion and tumefaction, catarrhal inflammation, ulceration or gangrene, with the clinical symptoms which belong to each."

To those less familiar than are the members of this society with the protean manifestations of this disease, it would seem that the subject of the etiology of appendicitis had been exhausted; but when in the light of our present knowledge we attempt an explanation of even the most notable phenomena of the disease we find how incomplete and unsatisfactory our knowledge is. Almost without exception writers on this subject have recognized the appendix as an atrophied rudimentary organ, poorly supplied with muscular power, and in consequence voiding its contents with more or less difficulty; its circulation as terminal and easily obstructed by causes which would produce little serious effect in other portions of the digestive tract, and its lymphoid tissues as of low vitality and of feeble resistant power. In connection with these factors, its dependent position, its communication with the cecum by an orifice more or less narrowed, with the consequent liability to impaction of feces, or foreign bodies and the entrance of infectious organisms, have accounted satisfactorily for the frequency with which this organ becomes diseased; but how little light this throws on the questions, Why is appendicitis so much more frequent between the ages of ten and thirty; in the male that in the female sex; in the Anglo-Saxon race? What is the influence exerted by climatic conditions and by heredity?

It is asserted that "in very early life the funnel-shaped appendix offers fewer opportunities for the formation and retention of masses of inspissated feces, while in old age atrophy of the mucous membrane about the cecal orifice again widens it, but we lack positive knowledge on these points."[3] If we accept the usual description of the anatomy of the parts concerned,

[3] The Amer. Text-Book of Surgery.

there seems to be no good reason why appendicitis should be found in men four or five times more frequently than in the female, but if future observation confirms the assertion of Clado, that a fold of peritoneum passes from the right ovary of the meso-appendix, the appendiculo-ovarian ligament, and if this fold carries a blood-vessel, an obvious and sufficient explanation has been found.

It has been shown (Bryant) that the male appendix is four-fifths of an inch longer than that of the female; that its caliber is slightly larger, and possibly as a result of the latter fact contains fecal concretions in a larger percentage of cases, but these circumstances do not seem to throw much light on the subject.

"The reasons advanced (Fowler) for this very decided comparative immunity of the female sex from appendicitis have been unsatisfactory heretofore. Morphological differences would naturally first attract the attention of the original investigator. The presence or absence of structural variations have not, to my knowledge, been determined as between the two sexes. Histologically, so far as I am aware, the appendix of the female is identical with that of the man. In its location and direction the differences are not sufficiently marked to even base a theory upon. The nerve supply is believed to be precisely the same in the two sexes.

"The existence of a process of peritoneum passing from the right ovary to the meso-appendix (the appendiculo-ovarian ligament of Clado) *was not demonstrated to exist* in but a *single* instance in *ten cases* studied with reference to this point. When present it is believed to assure some degree of immunity against the disease by increasing the blood supply and thus increasing the local vital resistance.

"The only other anatomical variation as occurring between the sexes which has been noted, is that relating to the arrangement of the lymphatic vessels. Between the folds of the appendiculo-ovarian ligament of Clado, the latter observer has noticed the existence of lymphatic channels which establish a communication between the appendix and ovary. Whether a communication between the lymphatic vessels of one organ and those of another may serve in affording protection of either the one or the other against diseased conditions can not, in the light of our present knowledge,

be intelligently discussed. While, generally speaking, the lymphatic vessels of the appendix pass directly into the appendicular lymphatic ganglion which lies in the angle formed by the appendix and the cecum, this arrangement may vary, particularly in the case of the female. In at least one instance of appendicitis occurring under my observation, in a female child of eight years, there existed a chain of enlarged lymphatic glands along the free border of the meso-appendix. Some of these were as large as the tip of the little finger and were so located as to bring more or less pressure to bear upon the appendicular artery. The appendix in this case was gangrenous at its distal extremity."

In other words, we are to believe that the larger caliber of the appendix in infancy and old age offers fewer opportunities for the formation and retention of inspissated feces, while the larger caliber of the male appendix as compared with the famale makes it more liable to contain fecal concretions, and thus more liable to inflammation. But if fecal concretions only play a small part in the causation of the disease and are found with equal frequency in both sexes, even this accommodating theory is insufficient.

Again, a short mesentery causes dragging on the appendix and an interference with its blood supply; a long mesentery allows such freedom of movement that torsion must result. Truly, the appendix, like "man born of woman, is of few days and full of trouble."

However, Fowler, after a critical study of the conditions which govern the blood supply, a study specially directed to the presence or absence of a meso-appendix, concludes, "so far as I am able to judge from the examinations of appendices removed in a diseased condition, the disease occurs quite often in those individuals in whom a well-formed and vascular meso-appendix is present as in those in whom the mesenteric attachment is but slightly developed or altogether absent."

The freedom of the female sex from appendicitis is not accounted for by the supposed additional blood supply to the appendix, as the ligament of Clado has only been found to exist in about one woman in ten; and, if the observation just quoted from Fowler be correct, its presence would seem to make little difference. Admitting, however, that this ligament does exist more frequently and that it carries a blood-vessel, and that this

is a protection to the appendix, we would still be as far as ever from an explanation of the frequent occurrence of the disease at certain periods of life. If irritative conditions, such as are associated with constipation or diarrhea, dragging on the meso-appendix by distension of the cecum with gas or fecal matter, or the presence in the appendix of pathogenic bacteria, were of prime importance in the causation of appendicitis, it is difficult to understand why the disease should be most frequent about puberty, when the vital forces are most active, and when the factors above mentioned are probably less active than at any other period of life.

Do we not lose the key to the situation when we consider the appendix as a functionless organ, or that at most its function consisted only in the secretion of a little mucus? I take it that no one considers the function of the appendix as a vital one, or even of any great physiological importance, but is it reasonable to hold the tissues of the appendix subject to different physiological and pathological laws from similar tissues in other portions of the body? Have we any reason to believe that the lymphoid tissue of the appendix differs materially from the lymphoid tissue in other portions of the digestive tract, or is subject to other physiological and pathological changes, except as modified by its anatomical relations.

Clado[4] found the structure of the appendix similar to that of the large intestine, and, according to the same author, it must be looked upon as a glandular organ rather than an organ of absorption. Its mucous glands and lymphoid tissue are much developed, and in the normal state the appendix never contains fecal matter.

Ribbert[5], of Zurich, in a microscopical and macroscopical study of four hundred specimens, concluded that the appendix undergoes a process of retrogression during the life of the individual, which manifests itself in, first, shortening; second, changes in the histological structure of its walls, and, thirdly, spontaneous obliteration of its lumen. That in the newborn its length averaged $3\frac{3}{8}$ centimeters; up to five years, $7\frac{3}{8}$ centimeters; five to ten years, 9 centimeters; ten to twenty years, $9\frac{3}{4}$ centimeters; twenty to thirty years, $9\frac{1}{2}$ centimeters; thirty to forty

[4] Annual, vol. 1, '93.
[5] Annual of '94.

years, 8¾ centimeters; forty to sixty years, 8½ centimeters; over sixty years, 8¼ centimeters; the greatest length thus being between the ages of ten and thirty years. Its dimensions are relatively larger in the newborn than the adult. Twenty-five per cent. were found partially or completely obliterated; the shorter the appendix the more frequent its obliteration. This obliteration he considered a retrogressive process and not pathological. In the ninety-nine cases out of four hundred the percentage of obliteration according to age was: One to ten years, 4 per cent.; ten to twenty, 11 per cent.; twenty to thirty, 17 per cent.; thirty to forty, 25 per cent.; forty to fifty, 27 per cent.; fifty to sixty, 36 per cent.; sixty to seventy, 53 per cent.; seventy to eighty, 58 per cent. Thus we see that the appendix, after steadily increasing in size, reaches its greatest development between the ages of ten and thirty years. After this age retrogressive changes are marked and very constant, twenty-five per cent. being obliterated. This is in perfect harmony with the behavior of similar tissue in other parts of the body, notably the thymus, the solitary and agminated gland of Peyer, and the tonsils, all of which reach their greatest development at or before puberty, and normally atrophy after this period.

The function of the vascular glands is now generally recognized as intimately concerned in the formation and preservation of the blood corpuscles. The almost constant presence in their tissues of larger quantities of uric acid as well as the nitrogenous bodies, xanthin, hypoxanthin, etc., than in other tissues less rich in nucleated cells; and the fact that these uric acid leucomaines occur as decomposition products of nuclein render the inference a fair one that some special nitrogenous matabolism must occur.

[6]"The opinion that the vascular glands serve for the higher organization of the blood is supported by their being all especially active in the discharge of their function during fetal life and childhood, when for the development and growth of the body the most abundant supply of highly organized blood is necessary. The bulk of the thymus gland in proportion to the body appears to bear almost a direct proportion to the activity of the body development and growth; and when, at the period of puberty, the development of the body may be said to be complete, the gland

[6]Kirke, Hand-book Physiology.

wastes and finally disappears. (The spleen more nearly retains its proportionate size and enlarges nearly as the whole body does.) Although the function of all the vascular glands may be similar in so far as they may all alike serve for the elaboration and maintenance of the blood, yet each of them probably discharges a peculiar office in relation to the whole economy and to that of some other organ."

Not only do we find this close analogy in the development of the lymphoid tissues of the appendix and similar tissues in other situations, but we find it likewise in the disorders of these structures. Take the tonsil, for example. In speaking of the predisposing causes of tonsillitis,[7] Delavan says "the first and most important factor seems to be youth, since it is most prevalent between the age of fifteen and twenty-five." It is rare in early childhood and after fifty. McKenzie, out of 1,000, found 601 occurred between ten and thirty; Delavan found 165 out of 260. McKenzie believes "that sex is not without influence in producing chronic hypertrophy of the tonsil, for out of the 1,000 cases 673 were males and 327 females." Delavan, out of 260 cases, 169 were females and 91 males; 162 of the 169 females were under thirty years of age, while of the males, 84 out of 91 were under thirty.

"Hypertrophy of the tonsil greatly increases the liability of the individual to acute attacks of tonsillitis. Sometimes this seems to be due to retention of excrementitious matter in the enlarged lacunæ, which acts as an irritant to the tissue and excites inflammation; and again the tonsil seems, in many cases, to be a vulnerable spot which is apt to sympathize with various irregularities of the body and to be subject to inflammation as the result of dyspepsia, the strumous diathesis, and, most important of all, rheumatism and gout. General conditions of ill-health may predispose to tonsillitis. It may be caused by mental depression and by unusual care and anxiety. Exciting causes are exposure to cold and wet; there can be no doubt, however, that septic influences often play an important part in their production, but it is highly probable that without some predisposing general condition the chilling of the surface of the body through exposure to cold would have little effect. The disease is more prevalent

[7] Encyloped. Dis. Chil., Keating.

during the spring months than the three winter months; finally, it may arise from various traumatisms, such as wounds, impaction of foreign bodies in swallowing; and from the irritation due to secretion in the tonsillar crypts."

Again, the same author says, "In many cases the tendency to tonsillar inflammation seems to be directly hereditary and not referable to any mediate condition, for while in such instances it might be supposed that the presence of such an inheritance might be due to the existence in parent and child of a common diathesis, the rheumatic for instance, nevertheless more than one case has been known to the writer in which no such diathesis could be traced. Climate may also play an important part."

To go back to appendicitis: At least four years ago my attention was first attracted to a seeming connection between the so-called rheumatic diathesis and the occurrence of appendicitis. I was forcibly impressed by several cases in which tonsillitis or other manifestations of the rheumatic diathesis were associated with or followed disease of the appendix, and also with the apparent beneficial results of treatment directed to this condition.

The belief that there was some connection between disease of the appendix and some general constitutional conditions was further strengthened by noting the occurrence in more than one instance of the disease in several members of the same family; the frequent occurrence of the disease under certain atmospheric conditions; and finally, by the frequency with which a history of unusual muscular exertion, fatigue, and exposure to cold and wet preceded the appendix trouble. Several of these points have been noted by other observers, but not satisfactorily explained.

Talamon[8] reports instances in which appendicitis occurred in several members of the same family, and refers to similar instances reported by other authers, but does not attempt to explain wherein the hereditary predisposition lies; whether in the length of the appendix, its breadth, or its structure, or in the disposition of Gerlach's valve. To his mind the frequency of appendicitis among the Anglo-Saxon race can not be explained by peculiarities of their habits of living.

Deaver[9] says, "I have had cases due to exposure to cold and wet. In one the attack was caused by taking a cold shower just

[8] *Med. Mod.*, 1896, vol. 9; *American Medico-Surgical Bulletin.*
[9] Treatise on Appendicitis.

after coming out of a warm bath; another was the result of wet feet, and a third from being chilled by lying in a cold room shortly after a heavy meal."

While looking up the subject of the appendix vermiformis Dr. North[10] had been startled by the number of cases of appendicitis reported and referred to. In seeking the explanation he had visited the health office of Brooklyn and studied the relative number of deaths for the several years since 1880 from peritonitis, perityphlitis, typhlitis, appendicitis, intussusception, obtruction of the bowels, colic, perforation of intestine, ulceration of bowels, perforation of appendix, and constipation. The percentage of deaths from these combined causes had been, in 1880, 1; in 1888, $1\frac{1}{4}$, and for the successive years to 1895 it had been $1\frac{1}{3}$, $1\frac{1}{10}$, $1\frac{1}{4}$, $1\frac{1}{3}$, $1\frac{1}{2}$, $1\frac{1}{3}$. It was obvious that since there were more deaths from these causes there must be more cases in the aggregate, else the treatment was faulty. It was not likely surgical technique would much further diminish the death-rate from operative interference, and Dr. North thought the difficulty lay in practitioners giving up as soon as a patient complained of a pain in the right side and calling in a surgeon, instead of resorting to early local antiphlogistic and internal remedies.

It would have been more charitable to the surgeon and nearer to the truth in my estimation, had Dr. North concluded: Notwithstanding the improvement in surgical technique during the past five years and the great number of lives saved by operative interference, the percentage of mortality from appendicitis has increased. This can *not* be explained by the small percentage of deaths from *operative* interference and due to *preventable* causes; and would not be effected by the much *larger* percentage of deaths due to *delayed operation* where the usual *medical* treatment had been employed, and obviously can only be due to a vastly increased number of cases occurring during these years from some unknown cause. And I would suggest that the epidemics of influenza during these years bear a casual relation to this great increase.

Haig[11] gives the notes of a case of Garrod's. It was that of a very gouty man, aged fifty, in whom, after exposure to cold, gout retroceded to the intestines, producing intense inflammation of

[10] *Medical Record*, Nov. 24, 1896.
[11] "Uric Acid as a Factor in the Causation of Disease."

the last eighteen inches of the ileum, as found after death, and also of a case recorded by Prof. Hayem, where enteritis occurred, the villi being strewn with small uratic incrustations, and he continues:

"Such a concentration of urates in the fibrous walls of inflamed intestine just as they concentrate around the lower alkaline fibrous tissues in joints, spleen, and kidney, in several of which they may be present in sufficient quantities to be visible to the naked eye, constitutes what I have spoken of as gout of the intestine, and forms, I believe, the anatomical condition behind such troubles as colic, enteralgia, and not a few cases of typhilitis."

At the risk of being unduly tedious, I shall quote some further observations of Haig. He says: "My clinical and experimental experience have led me to believe that a very large number of cases, such as I have mentioned, are neither more nor less than a gout of the walls of the intestinal tubes, and that a knowledge of their true pathology places us at once in a position to effect a complete and satisfactory cure by the use of the same drug which in my hands gives the best results in cases of arthritis due to uric acid, and I shall further point out that such colic or enteritis can be produced by giving certain drugs, all of which have the same action on uric acid, viz., that of driving it out of the blood into the tissues." Prominently among these drugs he mentioned mercury. "As in several other matters connected with gout, it was my personal experience that first directed my attention to the points that I am now bringing forward. Some eight or nine years ago I noticed that when I was suffering from some gastro-intestinal trouble, such as that which commonly produces an attack of uric-acid headache, and that when I treated this trouble by taking a small dose of calomel I sometimes produced pretty severe intestinal pain, which was generally located in or about the right iliac fossa. On one occasion, when a small dose of calomel, one grain, produced slight pain in this way, I thought that the purgative action had been insufficient and that a larger dose was indicated; the result of this, however, was to produce very severe pain indeed, which confined me to bed and the house for several days and made me quite unhappy about myself, as I feared that I had typhlitis. At this time, however, I knew very little about gout of the intestines, and nothing at all about the solubility of the urates of mercury, hence, beyond a mental note to avoid as far as possible the use of calomel for the future, the lesson was lost upon me. A year or two later, when taking some cocaine for purposes of experiment, I was surprised to find that it was followed on several occasions by somewhat similar pain, and this pain, which was partly due, I

think, to cocaine and partly the result of cold and occasionally wet feet late in the autumn, became chronic with relapses, and awakened my old fear of typhlitis and serious organic disease. So much was this the case that I consulted a friend on the matter, and at his suggestion was making up my mind to take several months' rest and change of climate when I chanced, still following out my experiments to some extent, or possibly prompted by some previous experiences, to take a few doses of salicylate of soda, and the effect was magical; pain was better soon after the first dose, and in two days was gone for good and all.

"I now began to see that I was not suffering from serious organic disease, but from a gout of the cecum accompanied by a certain amount of colic or enteralgia and enteritis, and when I afterward found out the insolubility of the urates of mercury I was easily able to understand why this metal had produced the pain on a previous occasion and why salicylate of soda had cured it so completely on this last occasion.

"Since this time I have had no further anxiety on the score of this intestinal disorder; I have often had it, and will undertake to produce it any time by the use of any of the other drugs I shall mention presently, but I have now complete confidence that I can put an end to it in a few hours' time by means of salicylate of soda. I have also treated several cases that were clinically typhlitis in the same way, and have every reason to be satisfied with the results.

"One of the most recent of these was in the person of a relative of my own, who is a member of the profession. I happened to hear that he was ill with what sounded like typhlitis, and I also heard that he had taken a dose of calomel before the attack began. It at once struck me that this was a repetition of my own experiences, and I went to see him as soon as I could. I told him what I had found out in my own case, and persuaded him to let me add a little salicylate of soda to the mixture he was taking. The result was in every way as satisfactory as in my own case.

"He at once began to improve, and in two or three days was up and about, while prior to the administration of this drug it appeared only too probable that his illness would be a matter of weeks. The history of this case is as follows: After one or two rather extensive dinners and champagnes he had a little disturbance, and with the intention of putting this right he took a few grains of calomel, and a few hours later was seized with violent colicky pains in the right iliac region. The pain came in attacks which were worse at night and caused nausea; there was an ill-defined fullness with tenderness in the right iliac fossa,

and temperature about 100° F. He asked a neighbor to come to see him, and lay in bed often groaning with pain, and with warm poultices constantly applied to the painful region; he took a carminative mixture, and a nurse was obtained for him; this was the condition of things when I went to see him, and, with the concurrence of a neighbor who was looking after him, added salicylate of soda to the mixture, with the result mentioned.

"There was, I think, no doubt in the minds of many of us that we were dealing with typhlitis, or a condition so like it that it deserved to be treated with great respect; but there was also in my mind no doubt, from the history of its causation, but that it would yield at once to salicylate of soda, and this proved to be the case.

"I have mentioned the pain produced by cocaine, and cocaine also diminishes the excretion of uric acid; likewise acids, nux vomica, and sulphates, especially sulphate of soda, occasionally acting the same way, may cause some intestinal pain of a similar kind; they diminish its excretion in the urine, clear it out of the blood and drive it into the liver, spleen, and fibrous tissues, especially into the fibrous tissues that have their alkalinity diminished by any previous irritation or inflammation. They produce this effect on uric acid, either by forming insoluble compounds with it, as in case of the metals, or they diminish the solvent powers of the blood through the absorption of acids from the intestines by the lymphatics, thereby diminishing its alkalinity, and under slightly different conditions any of them may produce gout of a joint instead of gout of the intestines.

"No one, I suppose, will deny that there is a large amount of fibrous tissue in the walls of the intestines, and if the fibrous tissues in fascia, tendons, and joints are liable to have urates deposited on them when they have had their alkalinity diminished by injury or irritation, I see no reason why the fibrous walls of the intestines should not be affected in exactly the same way.

"Thus the case just quoted from Sir A. Garrod might have a causation somewhat as follows: A gouty man has some more or less acute intestinal irritation (of dyspeptic origin), causing some nausea; this caused uricacidemia; on this there unfortunately follows exposure to cold, which raises the acidity and drives the urate out of the blood again, and as in other cases a large amount of it goes into that piece of fibrous tissue which is most irritated and least alkaline, in this case the fibrous structure in the walls in the last eighteen inches of the ileum. This still further increases the irritation, acute gouty inflammation of this portion of the intestines ensues and becomes so serious as to cause death.

"I have no doubt that if after death an extract had been made of this portion of the ileum it would have been found to contain far more urate than any other portion of the intestine of the same weight, and we have seen from the case previously mentioned that the gout may go on to deposit of urate visible to the eye.

"I have recently had an opportunity of testing a piece of inflamed intestine for uric acid in the case of Alice C., age twelve, admitted under my care at the Royal Hospital for Children and Women on November 11, 1895.

"She had been suffering from appendicitis or perityphlitis for some three weeks, and this had probably gone on to local suppuration before she was seen. She was put on salicylate of soda, which was given by rectum when her stomach rejected it; but this did not produce any marked effect, and she died on the fifth day after admission, with general peritonitis.

"I am in doubt in this case whether she got enough salicylate, owing to the vomiting which was present on admission; or whether the salicylate failed because suppuration had already taken place, as in my experience it is quite useless in gouty arthritis once suppuration has set in.

"At the *post-mortem* a local abscess round the appendix was found which had burst into the general peritoneal cavity shortly before death.

"I then took a portion of the cecum with the appendix, at the seat of the local abscess, and also a portion of the colon from the opposite side of the abdomen, near the splenic flexure, and tested them for uric acid in the ordinary way.

"I found in the portion of cecum and appendix .053 grains to ounce of uric acid and xanthine, but in the splenic flexure so little that I could not feel certain that there was any at all, while in the extract of cecum the precipitate with nitrate of silver was quite visible.

"I think it probable that the pus of the local abscess would have contained more uric acid had we been able to get it, and that the inflamed intestine would have contained more earlier in the disease.

"I should lay absolutely no weight on my results in this single case, but report it here merely for the purpose of getting others to repeat my observation whenever they have a chance, either in perityphlitis or the colic produced by lead or other metals.

"Again, we have some evidence pointing in the same direction in the part of the intestine commonly affected. Why should the last eighteen inches of the ileum, or, in my experience, the cecum and lower ileum be the parts affected?

"I would suggest that the reaction of the intestinal contents has something to do with it; it is well known that those of the large intestinal have an acid reaction, and it is not improbable that the alkalinity is diminished in the small intestines before the ileo-cecal valves are reached.

"Again, Bouchard[12] has shown that in certain dyspeptic conditions, especially in dilatation of the stomach, there is an excess of acid throughout the whole intestinal canal, and such acidity may cause local irritation and thus form the starting point for a concentration of urates in the intestinal walls and an attack of gout.

"Then any local irritation due to impacted feces or foreign bodies may act in the same way, setting up a local inflammation with fall of alkalinity which is soon complicated by a concentration of urates on the irritated spot; in this way the irritation in the vermiform appendix may precipitate a local attack of gout which, as in other parts, the joints and the valves of the heart, for instance, recurs and recurs, till a more or less extensive lesion (perityphlitis) has been produced.

"I notice that recent writers on this subject generally make use of the term appendicitis; and if proof is forthcoming that the trouble generally originates in the appendix there is no objection to this. As regards its gouty or rheumatic origin, it makes no difference whether it begins in the appendix, the cecum, or the lower ileum, as in the case reported by Sir A. Garrod; the only thing that concerns us is that these portions of intestine contain fibrous tissues, upon which urates may be precipitated if their alkalinity is diminished by such things as dyspepsia, cold, or irritating substances. And the irritation so caused may recur and recur and lead on to ulceration and sloughing just as in any other fibrous tissues."

"One swallow does not make a summer," nor does the fact of Dr. Haig having colic after a dose of calomel, and his relative recovering from a supposed typhlitis, after having taken a certain quantity of salicylate of soda, prove that either had a deposit of urate of mercury in the fibrous tissues of the intestine, which was removed by the salicylate, nor does the finding of considerable quantities of xanthine bodies in the inflamed tissues of the child Alice C. prove that there had been a gouty deposit in the fibrous walls of the intestine, for we know that adenine and guanine are normal constituents of the cell nucleus and are readily converted into hypoxanthine and xanthine respectively, during the process

[12] "Lecons sourles Auto-intoxications," p. 172.

of putrefaction, and consequently may be found in all suppurating tissues where nucleated cells are abundant; but these cases are *suggestive*, and we know it to be a fact that a deposit of urates may and does take place in the lower part of the ileum and the cecum under some circumstances, as evidenced by the cases reported by Garrod, Hayem, and others, and it is not at all improbable that such a deposit does *occasionally* cause sufficient irritation to start what may become, through infection, a fatal inflammation.

The causation of appendicitis by such a gouty deposit would naturally be expected to occur more frequently, as in the reported cases, in males after middle age, and may account for woman's relative immunity from this disease, but *only* in *just* such *measure* as is she *relatively free* from *other forms of gout.*

I have quoted these cases in detail mainly for two reasons. First, I wanted to direct your attention to the *fact* and *manner* of the occurrence of these gouty deposits, but at the same time to the fact that such *gouty deposits* do not, like *appendicitis*, belong to *early* life; and to suggest at this period of life, it is the presence of the large amount of *lymphoid* rather than fibrous tissue in the last eighteen inches of the ileum, the cecum, and the appendix that determines the frequency with which it becomes the seat of disease. Secondly, to emphasize the *unquestionable fact that no matter what the primary cause of the appendicitis may be, that neither salicylate of soda, opium, nor any other drug will restore the circulation in a disorganized appendix, prevent the leakage of intestinal contents or delay the inevitable consequences following the rupture of an encysted appendiceal abscess into the peritoneal cavity.*

The occurrence of appendicitis after violent muscular exertion has been noted by numerous writers and attributed to torsion of the appendix. In a paper read before the Kentucky State Medical Society in June, 1894, Dr. A. M. Cartledge says: "My observations, confirmed by others, that external violence from falls, blows, and contortion of the trunk may cause rotation of the appendix and twisting of its mesentery lead to another explanation of the frequency of appendicular disease in males, viz., the occupations of the two sexes." "That torsion alone by cutting off the blood supply is a cause of destructive changes in the appendix there can be no doubt. One such case, operated

upon a few hours (five) after the accident by Dr. J. S. Chenoweth, demonstrated the twisted appendix perfectly. I have seen undoubted evidence of such a condition in cases operated upon after infection and perforation."

In the discussion following this paper one member is reported as saying: "If the case be appendicitis, and you inquire into the cause, you will find there has been something in the occupation of the man that predisposes to it. To illustrate, I have had four cases within the last year, two caused by the men using a wood-saw. If a man who is not accustomed to using a buck-saw uses one vigorously, and has colic the next day, you may put it down that it is a case of appendicitis. The third case was caused by a man following a pond-scraper, and the fourth by riding a horse. Exercise is one of the points to be taken into consideration in the causation of appendicitis. If it is appendicitis, a violent exercise produces it; if it is a colic, it is imprudence in diet. I am perfectly satisfied that in following a pond-scraper, using a buck-saw, and riding horseback, the anatomical relations are such that we have in these forms of exercise an important point which may enable us to make an early diagnosis."

That the difference in the occupations of the two sexes does exert some influence upon the relative frequency of appendicitis in the sexes I take to be a fact, but I question whether it is through an increased liability to torsion of the appendix in the male. The case referred to by Dr. Cartledge, in which, five hours after the development of the acute symptoms, I found a gangrenous appendix twisted at its base, I have thought over many times in all its bearings. I believed at the time that torsion of the appendix was the primary factor in the disease process. In the light of subsequent experience and thought I question very much whether the sharp twist in the appendix was the *cause* rather than the *result* of the *necrosis*.

It would certainly seem that the few cases in which an acute twist of the appendix has been found, whether viewed as a primary factor in the process or secondary to necrosis of the appendix, would be at least offset by the possible nutritive disturbances in the appendix occurring in the female during pregnancy, from displacements of uterus and ovaries, or from the pressure of uterine and ovarian tumors. We have noted that the tonsils, com-

posed of very similar tissue to the appendix, are most subject to inflammation at those seasons when sudden alterations of temperature are apt to occur. And as previously intimated, although I can find no statistics on this point, I believe from my personal observations that the same will prove true of the appendix, and that there is something more than mere coincidence in the familiar grouping of these cases.

Diseases of both these organs occur more frequently in men than in women, and occur at the same period of life; are both as a rule associated with or preceded by intestinal disturbances; from their anatomical situations are alike subject to traumatism from impaction of foreign bodies or retained secretions, and are alike prone to bacterial infection.

The influence of heredity upon ultimate disease of the appendix can be reasonably accounted for, as in the case of tonsillitis, by the presence in parent and child of a common diathesis, the strumous or rheumatic, with a resulting tendency to hypertrophy and hyperplasia of the lymphoid glands at puberty, a most active predisposing cause of acute inflammatory attacks.

Let me call your attention to some other common affections usually considered as dependent upon the rheumatic diathesis, which my personal experience has convinced me are not infrequently associated with appendicitis and dependent upon the same general causes.

Speaking of valvular heart lesions, the author[13] says: "In 118 cases there was absence of rheumatic history in 40; in 10 of these chorea was manifest; in 13 there was no evidence of any antecedent or probable cause of the valvular trouble. Signs of rheumatism may be very slight in a child, skin eruptions constituting the only obvious signs of rheumatic condition, notably erythema, more rarely purpura or chorea or recurring bronchitis or asthma."

Bowen (quoted by Morrow) in speaking of purpura and acute circumscribed edema, says: "The close relationship and even interchangeability of certain of these cases of purpura with urticaria, with erythema, nodosum, and with angio-neurotic edema, favor the suggestion that the entire group may depend upon some poison, an alkaloid perhaps, the result of faulty chylo-poetic

[13] Keating, Ency. Dis. of Children.

metabolism which in varying doses in different constitutions excites in one urticaria, another peliosis rheumatica, a third fatal purpura."

"Purpura occurs more commonly in the young. According to Gintrac one hundred cases were observed before twenty years of age, ninety in five subsequent decimal periods. The blood changes observed in purpura were diminution in the quantity of red blood cells and solids, in constant variations in fibrin, which was diminished in infectious diseases, and purpura hemorrhagica, and increased in scurvy and purpura simplex. An increase of the white cells, a change in form of the red cells, the presence of embryonic elements and bacteria, and lastly fatty degeneration and inflammation of the small vessels, vascular dilatation and stasis. The disturbance of the capillary system and increase of blood tension should be considered to arise through vaso-motor disturbance of innervation. Hemorrhage may occur into the skin or mucous membrane, epistaxis is frequent, hematemesis is less so. When it does occur it is generally accompanied by pain in the left hypochondrium and splenic enlargement, and the stools sometimes contain blood; hematuria, hemorrhage from lungs and intestine, or cerebral hemorrhage may occur. In purpura rheumatica there is pain in the fibrous tissues of the joints from effusion or hemorrhage into the joints. A variety of so-called rheumatic purpura is not infrequently met with when in addition to the rheumatoid pain there is violent epigastric pain and colic; the pain being followed not infrequently by bloody vomiting and bloody stools."[14]

The frequency of these cases has lately been called attention to by several authors, notably Osler, who considers them as the visceral manifestations of exudative erythema. We find that with these disorders the history of one is the history of all. They are pre-eminently diseases of adolescence; they seem to occur more frequently in women than men, most frequently between twenty and thirty; may be produced under favorable conditions in certain individuals by many drugs, various articles of diet or disturbance of the digestive and generative organs, malaria, trauma, mental or bodily fatigue, or chilling of the surface of the body, and are almost without exception markedly influenced by the seasons, being more prevalent in early spring and fall and in

[14] Keating, Ency. Dis. of Children.

cold, damp seasons. A predisposition to these disorders seems to be hereditary; but, as with tonsillitis and appendicitis, it is highly probable that without some predisposing general condition the chilling of the body, etc., would have little effect.

I would like to call especial attention at this point to the striking similarity in the blood changes found in these cases of purpura rheumatica to those observed in appendicitis, viz., increased leucocytosis, fatty degeneration and inflammation of the small vessels, vascular dilatation and stasis, the disturbance of the capillary system and increase of blood tension being considered to arise from vaso-motor disturbance of innervation. Another point: if such vaso-motor circulatory disturbances, varying from a mere temporary congestion to actual hemorrhage, may take place in the brain, lung, joints, skin, kidney, stomach, and colon, why not much more rapidly in the vermiform appendix, considering that its circulation is so easily and disastrously disturbed by causes insufficient to produce such disturbances in other parts? We may put the question in another way: If such circulatory disturbances occur in other portions of the digestive tract, as a result of general constitutional conditions, when similar pathological conditions are found in the appendix, why should we attribute them to local accidents alone, more especially when such an assumption utterly fails to account for their more frequent occurrence at a certain period of life?

Rheumatism, which is considered the typical manifestation of this constitutional condition, is attributed by Angel Money "to a retention in the system of fatigued products of nitrogenous metabolism, the nervous system forming the secondary element."

"Tonsillitis is very commonly the forerunner of rheumatism, and indeed some have claimed it as a part of the rheumatic process; but if this is the case it must often be its only sign, as there may be no other symptom of rheumatism either before or afterward; but tonsillitis, in my experience, is very often associated with conditions of fatigue and overexertion, and these are just the conditions which bring about considerable uricacidemia, and when tonsillitis with fever supervenes upon this it is hardly to be wondered at that we should have some joint pain or even acute rheumatism." (Haig.) "The curve representing the rise and fall of rheumatism by months, shows it to follow with considerable regularity the rise and fall of atmospheric temperature. The curve

for rheumatism follows the curve for tonsillitis. Clinical observers have noticed and recorded an apparent relationship between tonsillitis and rheumatism, and although most of them have concluded that the tonsillitis was rheumatic, the fact that usually tonsillitis precedes rheumatism seems to indicate that if there is a casual relation between the two diseases, tonsillitis is the most likely to stand as the first link in the chain." (Hare.)

"Acute rheumatism may be produced by any thing which produces a sharp rise of acidity or fall in the alkalinity of the blood at a time when there is considerable supply of urate in the circulation (uricacidemia); but if there is no urate a rise of acidity may produce little or no effect; hence, those who eat much meat and drink most beer and have in consequence most uric acid stored in their body will be most likely to have occasionally considerable uricacidemia, and when exposed to cold and wet, or the sudden onset of any fever supervenes upon this, acute rheumatism may result." (Haig.)

"Age has an important influence on another factor of uric acid arthritis, namely, the absolute quantity of uric acid that is formed, for while in an adult urea is formed in about the proportion of 3 or 4 grains per pound of body weight per day, and uric acid in its natural relation of one to thirty-five would be about .09 to .11 to a pound daily; in a child of three or four urea may be as much as nine or ten grains per pound and uric acid .27 to .30 grains to a pound. A child or young person is thus by nature placed much in the position of an adult who eats largely of meat." (Haig.)

"The daily formation of uric acid is large, and uricacidemia and the arthritic irritation, so far as they depend upon formation for supplies, are correspondingly easily produced. It is little wonder, then, that when young persons who have this extensive nitrogenous metabolism increase it by eating largely of meats, meat extracts, juicies, and essences, the introduction and formation of uric acid should be very great and the probabilities of resulting mischief considerable; and that, as pointed out by Bouchard, children fed on meats and meat extracts should often suffer from gastro-intestinal derangements, skin disease, and early migraine, and that rheumatism and its most serious manifestations should come early.

"Another point is, that in children and young persons (probably in consequence of their more active metabolism), slight disturbances will produce great increase of temperature, and rise of temperature means, as we have seen, rise of acidity, the two things (fever and acidity) being probably co-resultants of increased metabolism. Thus the extraordinarily rapid development of girls at the age of thirteen may quite account for their

liability to acute rheumatism about that age, as well as to chlorosis and anemia a few years later.

"Young persons then are, from the action of natural causes, often liable to have considerable uricacidemia, and, whenever external cold or light febrile disturbance supervenes upon this, a powerful rise of acidity will drive the uric acid out of the blood into the joints and other tissues, for these tissues no doubt share largely in any general fall of alkalinity.

"A child with gastro-intestinal disturbance and loss of appetite has a headache and slow pulse and the signs of uricacidemia. On this there follows exposure to cold and wet, a slight sore in the throat, a peridental abscess, or other cause of febrile movement, and the resulting fall in alkalinity quickly produces a multiple arthritis with endopericarditis and changes the picture to that of acute rheumatism." (Haig.)

In this way the production of acute rheumatism may be completely accounted for by the action of causes that are to be met with every day, and the wonder is that any children should escape an attack, but it is fortunately necessary that a good many causes should act together, and this can only occasionally be possible.

"Thus uricacidemia means a large excretion of urate, and where this has gone on for several days the amount in circulation will be reduced. Again, gastro-intestinal disturbance means diminished metabolism and lessened formation of urate, so that, unless external cold or febrile movement supervenes at an early stage, there will not be enough urate to produce the most severe effects on the fibrous tissues." (Haig.)

Whether we believe with Haig that uric acid is formed side by side with urea in definite proportion, and that any excess in the system comes from deficient elimination and excessive introduction in our food, or believe with Fothergill in an excessive uric acid production, as a reversion to a primitive formation, is of little moment to us at present. Whether or not we believe that certain cases of appendicitis, tonsillitis, purpura rheumatica, or exudative erythema and rheumatism itself are due to *one* and the *same* cause, and believe that cause to be *uric* acid, or attribute these disorders to *other products* of *metabolic activity*, is also of secondary importance. It suffices us to know that as a matter of fact the Anglo-Saxon race is especially subject to dyspepsia,

rheumatism, and gout; and the children of these dyspeptic and gouty individuals, whether as a result of heredity or of dietetic and climatic conditions, show a marked tendency to hypertrophy and hyperplasia of the lymphoid glands at or before the period of puberty, with a corresponding liability to disease of these structures about the same time; and that these structures, rich as they are in nucleated cells, are intimately concerned in the production or elaboration of the relatively larger quantities of nitrogenous products found in these individuals and at this period.

It is quite sufficient for our present purposes, when we recognize the various conditions which favor the excretion or cause the retention in the system of waste products, or interfere with their elaboration, to note their constant relation to the disorders which we are considering, and that when by diet, drugs, or what not, we control the introduction and excretion of these leucomaines we largely control these disorders.

With this knowledge we have a most reasonable explanation of the part played by heredity in the production of appendicitis, as well as that by dietetic and climatic conditions, and an obvious explanation of its frequency in the Anglo-Saxon race is presented. The frequency of the disease between the ages of ten and thirty is seemingly due to several factors. As previously noted, the lymphoid tissue in the appendix, like that of the tonsil, normally reaches its greatest development and function about the period of puberty, then undergoes like atrophic changes; it is a reasonable assumption that it may undergo similar hypertrophic and hyperplastic changes under like constitutional conditions. I have found this hypertrophic condition in several cases just before puberty in which operation was done sufficiently early to permit of its recognition. The same findings are recorded and commented upon by Fowler in his "Observations upon Appendicitis," although attributed by him to a supposed torsion of the appendix.

(Fowler.) "Reasoning from the findings in the group of specimens of diseased appendices furnished from my own operative work, already alluded to, another source of trophic disturbances would seem to be in progressive hyperplasia or chronic stasis through defective venous return.

"It is not to be denied that other causes are operative in producing necrosis of the mucosa without consequent infection, as,

e. g., angulation of the appendix, the presence of foreign bodies in the lumen of the parts (a very rare circumstance, however), enteroliths, etc. It may be definitely stated in this connection, however, all efforts to establish the existence of a specific bacterium which is responsible for appendicitis had failed; and it is now known that when microbic infection occurs it may be simple or mixed, and that several varieties of organisms may find their way into the peritoneal exudate at once. This goes far to prove the presence of other etiological causes than micro-organisms; this in its turn strengthens the assumption that the local disturbance of tissue nutrition and resistance are operative to the production of the inflammation.

"Consideration of the so-called relapsing cases of appendicitis throw a different light upon the whole subject, not only in its pathology but also in the practical deductions which should aid the surgeon in his decision regarding operative interference. The cases now under consideration behave in a manner entirely consistent with the microscopic and macroscopic findings. The meso-appendix is hyperplastic, and so also is the appendix itself the seat, in many instances, of progressive hyperplasia. Everywhere in the specimens derived from this class of cases were found new-formed connective tissue; and vessels regularly show hypertrophic changes involving sometimes all and sometimes one or two of their coats.

"Of the circulatory disturbances in the appendix it may be further said that oligemia will supervene where progressive obliterating endarteritis is at hand, or where torsion is severe, or where a foreign body is present in the lumen of the tube; while hyperemia may originate either from torsion upon the vein, or secondarily as a result of local infection. Both conditions may undoubtedly obtain as a result of nerve lesions. That these conditions may produce effects upon the vitality and resistance of the appendix has already been shown.

"In speaking of non-specific inflammation, it is not intended in this connection to convey the idea that bacteria play no rôle in the process, for it is beyond dispute that they always do. The point here lies in the effort to discriminate between appendicitis resulting from such organisms as tubercle bacilli and those forms of the disease in which several pyogenic organisms seem equally competent to produce the inflammatory condition, and do so in conjunction with the trophic changes.

"Summing up all the facts at our command, it is evident: (1) That appendicitis results primarily from circulatory and nervous disturbances which greatly lower the resistance of the part, and that the vascular and nervous disturbances are due either to immediate torsion of the meso-appendix or chronic progressive hyperplasia of the same.

"(2) That the nature of the inflammation in the given case will be, (*a*) catarrhal, (*b*) purulent, (*c*) fibrinous, (*d*) a combination of the above named, or (*e*) interstitial. These in turn will depend upon the degrees of circulatory and nervous disturbance, and upon the nature of the micro-organisms present.

"(3) It can now be certainly shown that, in the given case of acute appendicitis, this initial attack is resultant from sudden torsion, and it is not the first warning of a chronic infective meso-appendicitis with progressive trophic lesions of the appendix.

"The results of vascular obstruction are directly analogous to ulcus ventriculi, dependent upon endarteritis of the gastric vessels; those of trophic nerve lesions to perforatory ulcer due to trophic nerve lesions of an extremity.

"It has been already shown that the great mobility of the appendix and its mesentery render these structures liable to torsion, and it can scarcely be doubted that this stands in direct etiological relation with the vascular and nervous degeneration."

Given, then, at puberty (or preferably a little later when the lymphoid tissue is still present in considerable amount, but its resistance lessened by the retrogressive changes taking place), an hyperplastic appendix or tonsil, a relatively large quantity of the products of retrograde tissue change stored up in the tissues, and an impressionable nervous system, and we have the foundation of many cases of appendicitis, tonsillitis, and rheumatism.

Under such conditions let a boy indulge in an all-day bicycle run, a violent game of foot-ball, a hard horseback ride, a long tramp with dog and gun, or handle a fork in the hay-field on a hot summer's day (and I have seen appendicitis develop under just these circumstances), or even let him follow a pond-scraper or dally with the fatal bucksaw—only let him get hot and tired, and as a result of muscular exertion and excessive perspiration bring a large amount of fatigue products into his circulation, and let him follow this up with a hearty supper, the next day he is "bilious," digestion is imperfectly accomplished, and fermentative changes begin in the intestine, with the formation of more leucomaines and ptomaines which may be absorbed and afterward eliminated by the kidney or may be deposited in the tissues.

The hyperplastic lymphoid tissue in the lower portion of the ileum, the cecum, and the appendix has its burden doubled, while the absorption of the acids of fermentation may render the solu-

bility and elaboration of these substances more difficult. According to Brunton the effect of dilute acids on the small vessels is to cause their dilatation, with a tendency to increase the exudation of fluids from the vessels and produce edema of the surrounding tissues, and this might further complicate the matter. The irritation of the sensory nerves in the appendix by these intestinal and bacterial products would further increase the local congestion by the dilatation of its arterioles, while at the same time the reflex contraction of the vessels in other parts of the body would raise the blood pressure and increase the rapidity of the stream of blood in the locally dilated vessels; the swollen, obstructed lymph glands, their outlet already inadequate and pressed upon by the exudation, surrounded as they are by a dense and unyielding musculo-fibrous sheath, their vitality thus so lowered would offer but a fertile soil for the development of pathogenic bacteria, which with a few hours' time are only necessary to complete our picture of acute perforative appendicitis.

There is another important factor which we would naturally expect to be most active in the years immediately succeeding puberty, found in the retrogressive changes normally taking place in the appendix, as pointed out by Ribbert; these changes consist in shortening, changes in histological structure of its walls, and narrowing of its lumen, tending to complete obliteration. Deaver[15] ascribes this obliteration to pathological conditions, and quotes Ribbert's findings to show its frequent occurrence, but fails to note Ribbert's unavoidable conclusion that this change was not pathological, but the normal retrogressive process, which takes place (not in the life of the race, but in the life of the individual). As previously suggested, the retention and inspissation of fecal matter doubtless results from some such narrowing of the lumen of the appendix and not from lack of muscular development; and as the lymphoid tissue is irregularly distributed these strictures may occur at several points.

From the greater amount of lymphoid tissue usually deposited about the orifice of the appendix we would expect stricture most frequently at this point. Some members of this society may recall in this connection the first appendix that I exhibited to this society, in which this condition was beautifully shown. The

[15] "Treatise on Appendicitis."

liability to accidents from the retention of fecal matter or secretions during this stage of retrogression would be in inverse ratio to the age of the individual, the percentage of obliterations of the lumen of the appendix increasing directly with age.

Why does appendicitis appear four times as often in men as in women? This is about the proportion as given by most writers, but it is very probable that this is too high, as many mild cases especially are apt to be overlooked in the young female and during pregnancy.

Rheumatism, gout, and tonsillitis are more frequent in the male, all ages considered, but rheumatism is more frequent in the female from about twelve to fifteen years of age, while purpura rheumatica and its allied affections are more frequent in the female at a little later period. If all these affections are influenced by the same general conditions, why should appendicitis alone occur with greater frequency in the male at all ages (admitting for sake of argument that it does)? The male appendix averages four fifths of an inch more in length than the female; its caliber is larger, and it is more liable to hypertrophy or hyperplasia. It would consequently be more liable to circulatory disturbances and acute inflammation. The obliteration, partial or complete, of its lumen would not occur so early, and its originally larger caliber and greater length would increase the chances of the retention of fecal masses as this narrowing of the lumen progressed.

The general habits of life (diet, exposure to weather, exercise,) of the two sexes may also render the male more liable to the disturbing influences which would bring about disease of the appendix.

The ligament of Clado, when it exists, would seem to me to be rather a detriment than otherwise, and would increase the liability of the individual to disease of the appendix, in that the appendix would be more than likely to participate in the circulatory and septic processes so frequent in the pelvic organs, or have its functions interfered with by traction from displacements of these organs, or from the assaults of the progressively aggressive gynecologists. (They have been accused of all the other crimes in the calendar, we might add this.)

We must consider another marked difference in the sexes,

however, than these mentioned. The development of girls, as shown by the annual increase of weight, as well as by other signs of metabolic activity, is greatest about the thirteenth year, and takes place very rapidly and precipitately, while with boys this development is much more gradual, and not obtained until the sixteenth year, and this yearly increase in weight in the male continues, although in lessened amount, for several years later.

"This very rapid growth and development in girls (according to Haig) entails a corresponding rapidity of tissue change, with a very large formation of uric acid and urea per pound of body weight, this being always much greater in the child than in the adult. But high urea formation is always accompanied by high acidity, that is to say, the urine will be highly acid and the blood lowly alkaline. The blood alkalinity being low it will be but a bad solvent of uric acid, and hence a considerable portion of the large amount of urate formed in these years of active metabolism will not be held in solution in the blood and excreted, but will be retained and deposited in various parts of the body, giving local signs of which we will speak presently.

"Unfortunately, later on, a girl's metabolism falls very greatly, and by the end of the eighteenth year her increase in weight is almost nil; with this there is a great fall in the formation of urea and of acids, and the blood becomes more alkaline; as a result of this it becomes also a better solvent of uric acid, and it now takes up and passes into the urine so much uric acid, probably several hundred grains, as was stored in the tissues during the preceding period of active metabolism, from twelve to fourteen; hence from sixteen to nineteen, or later, she will have an excess of uric acid passing through her blood and will suffer from its effects on the blood decimal, namely, chlorosis.

"Now I think that girls in their more early development will probably form more uric acid and urea per pound than boys in their later development, and when later on the girl's increase is almost nil, the uric acid previously retained will pass through the blood both in greater quantities and more suddenly than it does in boys, whose increase is for several years later very considerable and their acidity not so low; I therefore add a line representing the probable effects of the girl's increase in weight on the formation of urea and acids, and a broken line below showing the effects of this on the excretion of uric acid, and from these we see at a glance that the chlorosis and anemia of eighteen are the result of the passage of an excess of uric acid through the blood, which again is the result of a previous storage of this substance from twelve to fifteen. Add to this that just at the

time when a girl's increase of weight is coming down, and her urea and acidity falling, menstruation is established; and that, even if this does not upset digestion and appetite, it often obliges girls to keep quiet for several days, so that its result is to still further reduce urea and acidity and still more markedly flood the blood with uric acid, thus completely accounting for the increase of her chlorosis and the functional troubles so often met with at the menstrual period."

We can thus account for the liability of girls about the thirteenth year to rheumatism, as well as to chlorosis and purpura rheumatica a little later on.

It seems evident that while rheumatism results from the sudden precipitation of urates (possibly influenced by the lactic acid or other products of muscular activity), tonsillitis and appendicitis and the vascular disturbances and the blood changes of chlorosis, which with the irritable condition of the nervous system (most marked in women about the menstrual period) are apt to result in exudations or hemorrhages, are due to the circulation of these suboxidation products in the blood for a variable length of time. It is interesting to note that these local disturbances are prone to occur in tissues that have acid secretions, and it is not improbable that the capillaries are mechanically obstructed by local precipitation as well as by being chemically irritated. That these more severe blood vascular disturbances are capable of producing acute attacks of appendicitis I know to be a fact, and that appendicitis is not infrequently produced in this manner I believe to be equally true. This opinion was forced upon me long before any explanation of its occurrence was apparent.

I briefly report two cases in which this relation of cause and effect was unquestionable in support of my positive statement of fact. The first was that of a boy, age fourteen years, taken sick early in the summer, a year and a half ago; this boy I had previously attended in two slight attacks of tonsillitis; his sister, twenty-four years of age, had been under my care on several occasions during a period of three years. She was chlorotic, suffered with dysmenorrhea, indigestion, and tonsillitis. Several times she sent for me, complaining of violent colicky pain, usually located in the left hypochondrium, and for which I could find no

assignable cause; on one occasion this was attended by vomiting and an outbreak of urticaria.

A second sister, seventeen years old, suffered two attacks of tonsillitis and a mild rheumatic attack two years ago; last year she stopped school on account of sick-headaches.

I first saw this boy about 12 o'clock in the day; he had been employed in a milk depot for about a week, and the day before my visit had done an unusually hard day's work for a boy of his age, handling the heavy cans, etc.; while overheated he drank quite a quantity of cold milk before he left the dairy, and the next morning awoke, nauseated, and with a sore throat. A little later a number of large erythematous wheals appeared over the body, and almost simultaneously he complained of a violent pain in the region of the appendix. A diagnosis of appendicitis was made at my visit a few hours later, the classical signs being all present; his temperature was 100.2° F., pulse 90. No remission of symptoms following the action of a saline and an enema, he was removed to the Norton Infirmary and operated upon at nine P. M. the same day. He was taken to the infirmary at the special request of his sister, who informed me that they were all completely broken down nursing her father (whom I had never attended), a man sixty-six years old, who was then in his fifth week of a typhoidal attack and in a condition of septic delirium. Ten days later, when the boy went home, I was asked to look at the father, who was still holding on; the typhoid proved to consist of an enormous collection of pus surrounding the remains of a disorganized appendix. The pus had worked up behind the liver and down under Poupart's ligament along the femoral vessels; a free opening, front and back, gave him relief, but his constitution was completely shattered, and he died eight months later.

On opening the abdomen of the boy the appendix was found pointing downward and partially overlapped by the cecum; its walls were hyperplastic and quite hard from the dense infiltration; the meso-appendix was thickened and extended almost to the tip of the appendix. The distal third of the appendix and the corresponding portion of the meso-appendix presented a dark, somewhat mottled appearance from extravasation of blood into this hyperplastic tissue; the lumen of the appendix was pervious,

though somewhat compressed, and contained only a little mucoid material and soft fecal matter. There was no torsion of the appendix, nor any other apparent mechanical obstruction to the circulation, and no reasonable doubt could exist but that the circulatory disturbance in the appendix and that taking place in the skin were identical.

Second case was in a boy, age fifteen, operated upon January 5, 1895. This boy's mother has suffered from tonsillitis and rheumatism; one aunt has had rheumatism, a second, exudative erythema. His father has been a great sufferer from rheumatism and migraine, and now has a heart-murmur. He also frequently shows evidence of nutritive disturbances in the skin by an outbreak of boils, which the most vigorous antiseptic treatment has always failed to relieve until used in conjunction with the salicylates, colchicum, etc.

I first saw this case in the fall of 1890; he was then suffering from tonsillitis and nose-bleed; from that time until the spring of '94 I attended him at various times with tonsillitis, nose-bleed, colic, and one attack of urticaria; none of these attacks were very severe. In May, 1894, after a horseback ride, he had a severe attack of colic, attended with vomiting; his pain was general over the abdomen, and unattended by any local tenderness or muscular regidity; his temperature was slightly above normal. His mother stated at the time that he had complained of pain, and had vomited after eating on several occasions in the week immediately preceding this severe attack; no appendicular trouble could be made out.

The following August he had a second attack, more severe than the first, and accompanied by fever and vomiting, with considerable pain in the right iliac region, which had passed off at the end of a week when I saw him. This attack followed a fatiguing ride out into the country. On November 22d following he started for a several days' hunt in Indiana. The first day out, the weather turning very cold, the frozen ground making walking very tiresome and uncertain, late in the afternoon he made a misstep and fell, cutting a deep gash in his hand, which necessitated a return home that night. Next day he had an attack of bronchial asthma, accompanied by nose-bleed. This attack lasted, with intermissions, until December 6th. On Jan-

uary 6, 1895, I was hurriedly called, to find him suffering from severe colic and vomiting. He was very nervous and rolling around over the bed; temperature 99.2° F.; pulse 100; abdomen was not distended; the pain was most intense under the border of the ribs on the left side and in the right iliac region; tenderness on pressure and rigidity of right rectus. No cause for the attack could be assigned. Enema of glycerine and water brought away only a little gas; calomel, gr. 1½, was retained, but saline was rejected. Five hours later he began to cough again and his nose to bleed.

Twenty-two hours after the commencement of the attack his temperature was 100.6° F.; pulse 105; he had vomited several times and his bowels had not moved. An increasing tenderness, etc., in the region of the appendix warned me against further delay, and notwithstanding many misgivings as to his general condition his abdomen was opened; the appendix immediately presented. There were no adhesions or other evidences of previous inflammatory trouble. The appendix, which was exhibited shortly afterward in this society, was three inches long, the mesoappendix extending about half its length; it was tensely distended, containing some muco-purulent fluid with fecal odor and a good-sized blood clot; hemorrhage had also occurred into the walls of the appendix, which were almost black in color and on the verge of rupture; there was no evidence of torsion. The case went on without special incident until the eighth day, when the stitches were removed from the very small wound, union being perfect. On the ninth day his stomach became deranged from some little error in his diet; this was followed by severe abdominal pains, chiefly in the left side; as he expressed it himself, the *region* of the *wound* was the *only place* that *did not hurt.* He became quite hysterical after this and presented every possible phase of purpura rheumatica: pain and edema in the muscles and joints, urticarial lesions of all styles, bleeding from the nose, stomach, intestine (always preceded by a severe colic), and the kidney; purpuric spots developed on the legs, but the rest of the body was free, perfect recovery finally taking place. Could the presence of the wound in the abdominal wall over the cecum, through reflex nerve action, have accounted for the freedom from pain in this locality, while he suffered repeated attacks in other portions of the abdomen?

Just in the midst of this affair his sister, a year younger, who was also subject to tonsillitis, nose-bleed, and rheumatism, while skating fell into an air-hole and became thoroughly chilled before her wet garments could be changed. This was quickly followed by an attack of fever, her temperature reaching at its highest point 104° F.; this lasted for three weeks and was attended by nose-bleed, some puffiness and pain about the knee-joints, erythematous nodes over the tibia, and an apparent swelling of the liver and spleen; a diagnosis of typhoid fever was made by two experienced consultants.

The question at once suggests itself, why, if these more violent vascular disturbances are more common in the female, should they involve the appendix more frequently in the male?

These disorders, we have noted, are usually brought on about the menstrual period, when this function is deranged, the metabolic changes disordered, and the nervous system in an irritable condition.

Brunton calls attention to the great difference existing between the vessels of the intestine and those in some other situations, noting the fact that the former are more under the control of the vaso-motor center, and that when this is stimulated they contract greatly; and further, that this may be produced by irritation of the vaso-motor center or the peripheral terminations—directly by the action of drugs, indirectly by the accumulation of carbon dioxide in the blood, and reflexly through the sensory nerves.

These conditions are so perfectly fulfilled in the dysmenorrheaic female that it is not surprising that she suffers at this period with vaso-motor disturbances, whether these are produced altogether through the vaso-motor system or in addition there exists an actual blocking of the capillaries from colloid precipitates, but it is not improbable that the irritating waste products and carbon dioxide accumulating in the blood would cause contraction of the intestinal vessels and diminish absorption and the functional activity of the intestine; the amount of blood in the intestinal vessels would doubtless be further diminished by the congestion of the pelvic organs and by the reflexes acting on the intestinal vessels.

This reflex influence on the intestine from an irritated ovary

was thought by Brunton to be a frequent cause of constipation in neurotic females, and the truth of this opinion is supported by the effect of small doses of opium in such cases, which by inhibiting or transferring this reflex nerve influence he found to exert a laxative action; and it seems to me altogether probable that this irritation of the ovary and uterus at the menstrual period and its reflex influence on the intestinal circulation may be another important factor in the relative immunity of the female at this time from circulatory disturbances in the appendix.

This might account for the infrequency with which the appendix is involved in comparison with other organs in women, the subjects of purpura rheumatica, but even admitting that no such influences exist, and that these acute vaso-motor disturbances when they do occur are as apt to involve the appendix of the female as that of the male, it is by no means certain that such disturbances occur so much more frequently in the female than in the male as to materially affect the general result.

The cases reported, however, in which exudation and hemorrhage took place into the appendix during the progress of an attack of purpura rheumatica in the two boys, while their two sisters, presenting much the same lesions in other situations, failed to develop any appendix trouble, are at least suggestive.

Another point to be taken into consideration is the relative infrequency of these severer vascular disturbances even in the female, for as a rule as soon as the menstrual functions are well established the susceptibility to these affections is markedly diminished.

Some light may be thrown upon the influence of menstruation upon appendicitis in the future by noting the frequency of the primary attack in women before puberty, during the sexual period, and after the menopause. The influence of pregnancy would be two-fold, first, through its influence on the metabolic processes; secondly, by the pressure effects of the rapidly enlarging uterus.

The points to which I would especially direct your attention are briefly these: We find no evidence to justify the assumption that the lymphoid glands of the appendix differ materially in their development and function from similar glands in the ileum and colon or other situations; therefore, in the absence of such

evidence I see no reason to doubt the findings of Ribbert in the four hundred appendices examined by him; nor the correctness of his conclusion that the appendix, by virtue of the lymphoid tissue of which it is largely composed, reaches its greatest development at puberty, and soon thereafter undergoes a process of retrogression, consisting of shortening, changes in the histological structure of its walls, and more or less complete obliteration of its lumen, similar atrophic changes being known to take place in other lymphoid glands at this same period.

We find no evidence to support the assumption that the lymphoid glands of the appendix are uninfluenced by constitutional conditions and other agencies which tend to bring about hyperplasia or acute inflammation of the tonsils or the lymphoid glands of the colon and ileum; therefore, when such changes are observed, taking place coincidently in the appendix and these other structures, we must conclude that the same conditions are at work rendering the soil favorable for bacterial invasion.

Again, we have noted the practical identity of the vascular and nerve lesions of appendicitis with those found in the intestinal lesions of exudative erythema and similar affections dependent upon the rheumatic diathesis. We find the same pathological conditions in ulcers of the skin dependent upon this same diathesis.

"Quenu[16] found in the microscopic study of the skin and other tissues in so-called varicose ulcers of the leg, the veins varicose, dilated, and surrounded by new connective tissue, which was forming and condensing at the same time. The arteries were affected by endarteritis and atheroma, and occasionally there was thrombosis of large branches. In the nerves there was a new growth of connective tissue, beginning around the dilated capillaries and surrounding the nerve fibers, which afterward degenerated on account of the pressure exerted by this tissue as it contracted. These alterations were found in nerves at a long distance from the point of ulceration, and even in those nerves which were not distributed to that part of the leg. He thinks the changes began in the vessels, then attacked the nerve, and finally caused trophic alterations and ulcerations of the skin. He believes himself able to

[16] Ref. Hand-Book Med. Science.

exclude an ascending neuritis secondary to the inflammation of the ulcer."

"Shrieder[17] investigated a number of cases of ulcer (that could not be ascribed to any specific cause) and found in the great majority of them evidence of atheroma, varicose veins, chronic bronchitis, skin eruptions, heart affections, headache, joint troubles, ribbed nails, and other symptoms of that peculiar constitutional vice known as gout or lithiasis by England writers. The cause or causes which produce this inveterate disorder of the system are as yet but poorly understood.

"But the extensive trophic changes which it occasions in all the tissues of the body form a reasonable basis for the hypothesis that it may also be responsible for the nutritive changes upon which depend the occurrence of ulceration in cases in which no more definite cause can be detected."

In the face of such evidence we can but conclude that the similar vascular and nerve changes found in the appendix are the results of nutritive disturbances of constitutional origin, and not secondary to torsion of the appendix and bacterial infection, as heretofore thought.

Strictures of the appendix may be due to inflammatory bands or to the contraction of cicatricial tissue, the result of previous ulceration, but certainly such an origin is most improbable in the majority of such cases, and it seems unquestionable to me that the great majority of these contractions are the result of the retrogressive changes taking place in the appendix after puberty.

The more frequent occurrence of appendicitis about puberty and in the years immediately following would strongly indicate the part played by the functional disturbances in this hypertrophied lymphoid tissue in its production.

Acute cases have been reported where the mucosa was extruded from its muscular sheath intact, which could scarcely occur if the whole blood supply to the appendix were cut off by torsion or the submucosa had become necrotic by means of infection through the mucosa which remained intact. In the present state of our knowledge, or, more properly speaking, ignorance, the vascular disturbances which give rise to necrosis of the lymphoid glands of the tonsil, cecum, or appendix, or in milder cases only to such nutritive changes that the lessened

[17] Ref. Hand-Book Med. Science.

resistance permits of bacterial invasion, seem to be brought about by, first, blocking of the capillaries by the precipitation of colloid nitrogenous bodies; second, disease of the walls of the small vessels from the presence in the blood of deleterious substances; or, third, vaso-motor disturbances, (*a*) irritation by chemical products, (*b*) reflexly. The important point to us just at present, however, is that these *vascular disturbances* are so intimately *connected* with the *rheumatic diathesis*, which we all recognize but do not as yet thoroughly understand. Whether calomel or any other drug can cause a precipitation of colloid bodies in the capillaries of the lymph glands by combining with their metabolic activity, just as such precipitation takes place in the products of the laboratory, is a matter purely of conjecture. This is equally true of the action of salicylate of soda in the removal of such deposits; but may we not find that it is by some such influence on the metabolic processes going on in these glands, rather than by their direct antiseptic action, depends the beneficial results of salicylate of soda, guaiac, and guaiacol in appendicitis, tonsillitis, and typhoid fever?

Finally, I would have you note the two cases reported in which actual hemorrhage occurred into the appendix during an attack of purpura rheumatica. I have been able to find one case in the literature of the subject where peritonitis and death resulted from necrosis and perforation of the stomach from such a hemorrhage into its walls, but no mention of even the possibility of such an acute vaso-motor disturbance causing hemorrhage and necrosis of the appendix. This, in my opinion, is not because such cases are so rare, but because they have been unrecognized. The consideration of the treatment of appendicitis has no place in this article, nor have I any suggestion at present to offer the members of this society, but for the benefit of those who stand less in awe of a necrotic appendix than do we, and who by my incidental allusions to the action of drugs might be encouraged to place undue reliance upon medicinal treatment in this disorder, I would recall the result in the case of the child treated by salicylate of soda that I have previously quoted from that most interesting work of Haig; and while I have never advocated immediate operation in all cases of appendicitis as soon as the diagnosis was made, regardless of time, place, or circumstances,

nor regarded the physician as possessed of less intelligence and diagnostic ability than the surgeon, I have always advocated an immediate diagnosis, and I would most earnestly insist that with our present knowledge of the frequency and the rapidity with which necrosis and perforation may take place in seemingly mild cases of appendicitis, and the almost inevitably fatal result following without immediate surgical interference, that the physician who treats an acute attack of appendicitis, even of mild character, without making provision for immediate operation, should the necessity arise, does his patient a grave injustice; and if he does not allow the surgeon, upon whom he will shift the responsibility of this operation and the ultimate result, to see the case at the earliest moment and have a voice in determining when this necessity does arise, he does both a grave injustice.

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